

Rec'd PCT/PTO 02 AUG 2005

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



10/544238



(43) International Publication Date  
26 August 2004 (26.08.2004)

PCT

(10) International Publication Number  
WO 2004/071384 A3

- (51) International Patent Classification<sup>7</sup>: A61K 31/46, (74) Common Representative: BOEHRINGER INGELHEIM INTERNATIONAL GMBH; Binger Strasse 173, 55216 Ingelheim (DE).
- (21) International Application Number: PCT/EP2004/001144 (81) Designated States (unless otherwise indicated, for every kind of regional protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date: 7 February 2004 (07.02.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
03002986.2 11 February 2003 (11.02.2003) EP
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- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
1 December 2005
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/071384 A3

(54) Title: NEW PHARMACEUTICAL COMPOSITIONS BASED ON ANTICHOLINERGICS AND TACE-INHIBITORS

(57) Abstract: The present invention relates to novel pharmaceutical compositions based on anticholinergics and TACE (TNF alpha converting enzyme) inhibitors, processes for preparing them and their use in the treatment of respiratory diseases.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/001144

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 A61K31/46 A61K31/4164 A61K45/06 A61P11/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, EMBASE, MEDLINE, CHEM ABS Data, WPI Data, PAJ, BIOSIS		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02/072095 A (BOEHRINGER INGELHEIM PHARMA ; DISSE BERND (DE)) 19 September 2002 (2002-09-19) the whole document	1-4, 12-28
Y	HELE D J ET AL: "NOVEL THERAPIES FOR THE TREATMENT OF INFLAMMATORY AIRWAY DISEASE" EXPERT OPINION ON INVESTIGATIONAL DRUGS, ASHLEY PUBLICATIONS LTD., LONDON, GB, vol. 12, no. 1, 1 January 2003 (2003-01-01), pages 5-18, XP009014907 ISSN: 1354-3784 page 6, column 2, paragraph 3 page 7, column 2, paragraph 2 page 11, column 1, paragraph 1 ----- -/--	1-4, 12-28
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family		
Date of the actual completion of the international search  21 September 2004		Date of mailing of the international search report  14 01. 2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  Leherte, C

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/001144

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>TRIFILIEFF ALEXANDRE ET AL: "Pharmacological profile of PKF242-484 and PKF241-466, novel dual inhibitors of TNF-alpha converting enzyme and matrix metalloproteinases, in models of airway inflammation" BRITISH JOURNAL OF PHARMACOLOGY, vol. 135, no. 7, April 2002 (2002-04), pages 1655-1664, XP001202131 ISSN: 0007-1188 abstract</p>	1-4, 12-28
Y	<p>HANSEL T T ET AL: "TIIOTROPIUM BROMIDE: A NOVEL ONCE-DAILY ANTICHOLINERGIC BRONCHODILATOR FOR THE TREATMENT OF COPD" DRUGS OF TODAY / MEDICAMENTOS DE ACTUALIDAD, J.R. PROUS SS.A. INTERNATIONAL PUBLISHERS, ES, vol. 38, no. 9, September 2002 (2002-09), pages 585-600, XP009022208 ISSN: 0025-7656 page 596, column 1, paragraph 2 - page 597, column 1, paragraph 1</p>	1-4, 12-28
Y	<p>XUE CHU-BIAO ET AL: "Design, synthesis, and structure-activity relationships of macrocyclic hydroxamic acids that inhibit tumor necrosis factor alpha release in vitro and in vivo" JOURNAL OF MEDICINAL CHEMISTRY, vol. 44, no. 16, 2 August 2001 (2001-08-02), pages 2636-2660, XP001199586 ISSN: 0022-2623 abstract</p>	1-4, 12-28

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>1 - 1460 - PCT</b>	<b>FOR FURTHER ACTION</b>		see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No.  <b>PCT/EP2004/001144</b>	International filing date (day/month/year)  <b>07/02/2004</b>	(Earliest) Priority Date (day/month/year)  <b>11/02/2003</b>	
Applicant  <b>BOEHRINGER INGELHEIM INTERNATIONAL GMBH</b>			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☒ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☒ none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2004/001144

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-4, 12-28 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4, 12-28 (all partially)

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with sl422  
---

2. claims: 1-4, 12-28 (all partially)

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with sp057  
---

3. claims: 1-4, 12-28 (all partially)

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with SC903  
---

4. claims: 1-4, 12-28 (all partially)

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with SE205  
---

5. claims: 1-4, 12-28 (all partially)

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with Ro-32-7315  
---

6. claims: 1-4, 12-28 (all partially)

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with BMS-561392  
---

7. claims: 1-4, 12-28 (all partially)

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with PFK 242-484  
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. claims: 1-3, 12-28 (all partially), 5

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with a compound of formula 2a  
---

9. claims: 1-3, 12-28 (all partially), 6

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with a compound as specfied in claim 6  
---

10. claims: 1-3, 12-28 (all partially), 7

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with a compound as specfied in claim 7  
---

11. claims: 1-3, 12-28 (all partially), 8

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with a compound as specfied in claim 8  
---

12. claims: 1-3, 12-28 (all partially), 9

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with a compound as specfied in claim 9  
---

13. claims: 1-3, 12-28 (all partially),10

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with a compound as specfied in claim 10  
---

14. claims: 1-3, 12-28 (all partially), 11

Pharmaceutical compositions, containng one or more anticholinergics, selected from among tiotropium salts, oxitropium salts or ipratropium salts, combined with a compound as specfied in claim 11  
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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/001144

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02072095	A	19-09-2002	DE 10111843 A1	19-09-2002
			CA 2440699 A1	19-09-2002
			WO 02072095 A2	19-09-2002
			EP 1385519 A2	04-02-2004
			JP 2004528305 T	16-09-2004
			MX PA03008223 A	29-01-2004
			US 2002193394 A1	19-12-2002
			US 2004039011 A1	26-02-2004
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